Accidental inhalation of mercury vapour: respiratory and toxicologic consequences

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Four adults, including a pregnant woman, and three children were admitted to hospital following accidental exposure to mercury vapour produced by heating mercury–gold amalgam. Initial symptoms and signs included a paroxysmal cough, dyspnea, chest pain, tachypnea, nausea, vomiting, fever and leukocytosis. Pulmonary function testing performed on the second day after exposure revealed air-flow obstruction and minor restrictive defects in three patients. The diffusing capacity of the lung for carbon monoxide was reduced in two of these patients. The mean initial blood mercury level (± one standard deviation) for the seven patients was 30.8 ± 1.5 μg/dl. A computer analysis showed mercury to behave as a two-compartment system, the compartments having half-lives of 2 and 8 days. The four adults received chelation therapy with D-penicillamine, which did not affect the urinary excretion of mercury. The pregnant woman's infant, born 26 days after exposure, had no detectable clinical abnormalities. The levels of mercury in the blood of the mother and infant at birth and 6 days later were comparable, indicating free transfer of the metal across the placenta.

Quatre adultes, dont une femme enceinte, et trois enfants ont été hospitalisés après une exposition accidentelle à des vapeurs de mercure produites par le chauffage d'un amalgame de mercure et d'or. Les premiers signes et symptômes incluaient une toux paroxysmale, de la dyspnée, des douleurs thoraciques, de la tachypnée, des nausées et vomissements, de la fièvre et une leucocytose. Les tests de fonction pulmonaire pratiqués le deuxième jour après l'exposition ont révélé une obstruction de l'écoulement gazeux et des troubles ventilatoires restrictifs mineurs chez trois patients. La capacité de diffusion des poumons pour le monoxyde de carbone était réduite chez deux de ces patients. Le taux sanguin initial moyen de mercure (± un écart type) pour les sept patients était de 30.8 ± 1.5 μg/dl. L'analyse par ordinateur a montré que le mercure se comportait selon un système à deux compartiments ayant des demi-vies respectives de 2 et 8 jours. Les quatre adultes ont été traités par chélation avec de la D-pénicillamine, laquelle n'a pas modifié l'excrétion urinaire du mercure. L'enfant que portait la femme enceinte est né 26 jours après l'exposition; il n'avait pas d'anomalie clinique décelable. Les taux de mercure mesurés dans le sang de la mère et du bébé à la naissance et 6 jours plus tard étaient comparables, indiquant un transfert libre du métal à travers le placenta.

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Despite the well known danger of exposure to elemental mercury vapour,[1-4] accidental exposure continues to occur at work sites and in dental offices, hospitals, nurseries and homes. A current and apparently popular practice among amateur prospectors involves heating mercury–gold amalgam to recover the precious metal.[5-7]

We studied the pharmacodynamics and the effects on pulmonary function of inhaled mercury vapour in three children and four adults accidentally exposed. Included was a woman who was 37 weeks pregnant and who was followed up post partum.

Case histories

At about 6 pm one evening in November a 28-year-old amateur prospector was attempting to recover a trace amount of gold by heating "a tablespoon" of mercury–gold amalgam to evaporation. This process, which is used to recover the gold dust, was done over a kitchen stove ventilated by a small fan ducted to the outside of the house. The man became ill, with a paroxysmal cough, dyspnea, chest pain, nausea and vomiting at about 8 pm, but he was unaware of the cause of the illness. His two children, aged 18 months and 7 years, and a 28-year-old male friend in adjacent rooms experienced similar symptoms at about 11 pm. Both adults and the children were taken to hospital at 1 am by the prospector's wife, who had been out of the home for the evening.

A 21-year-old man, his 19-year-old pregnant wife and a 16-month-old child occupied a basement suite in the same bungalow. They had no knowledge of the illness of the first family, but they began to suffer from identical symptoms at about 2 am. They were taken to the hospital at 4 am.

All seven patients were treated for nausea, vomiting and dyspnea. The

prospector's 7-year-old daughter, who was known to have asthma, was treated with salbutamol by inhalation. The four adult patients, but not the children, received chelation therapy with 250 mg of D-penicillamine by mouth four times daily from the 2nd to the 10th day following exposure.

Investigations

Pulmonary function studies were performed on the prospector and his friend and on the child with asthma 2 days after exposure and then 40 days later. Vital capacity, functional residual capacity and total lung capacity were measured by helium dilution on a Godart Pulmotest (Godart Instruments, Debiltutr, the Netherlands). The maximum mid-expiratory flow rate and the forced expiratory volume in 1 second were obtained from the spirometric curves. The single-breath diffusing capacity of the lung for carbon monoxide was determined on a Medicraft apparatus (Medicraft Instruments, New York), and prediction values for all of the foregoing data were obtained from the work of Bates and colleagues.[8]

Whole-blood mercury levels were determined by the cold vapour technique[9] in blood samples collected in heparinized tubes from the children and adults at various intervals after exposure as well as from two healthy adults living in the same region. Urine collections for 24 hours from the patients were also analysed by the cold vapour technique. The results of the blood studies were then computer analysed using a package program for regression analysis by fitting linear sums of exponential terms, developed by Cook and Taylor.[10]

Ambient mercury levels were measured in the house at intervals of 2 to 45 days with a calibrated Bacharach mercury vapour monitor (Bacharach Instruments, New York).

Observations

All seven patients presented with predominantly respiratory and gastrointestinal manifestations along with fever and leukocytosis. Most of the acute symptoms subsided within 12 hours, although some patients reported symptoms that were still present 28 days later. These symptoms included cough, a metallic taste and fatigue (in four patients), tremor and gingival discomfort (in three) and chest pain (in one).

Temperatures at the time of admission (rectal in the two youngest patients) ranged from 37.8 to 39.3°C but were normal within several hours. The leukocyte counts, initially 10.5×10^9/l to 22.5×10^9/l, subsided within 48 hours. Subsequent hematologic and liver function studies gave normal results. The prospector's two children showed a reduction in creatinine clearance to 46 and 51 ml/min·m^{-2} despite normal urea nitrogen levels of 5 and 8 mg/dl (urea levels 1.8 and 2.8 mmol/l) and serum creatinine levels of 0.3 and 0.6 mg/dl (26.5 and 53.0 μmol/l) respectively. However, this abnormality had resolved when they were examined 28 days later.

Four of the seven patients (the prospector, his two children and his friend) had rhonchi or crepitations that were either localized or generalized. The child with asthma, who initially had normal breath sounds and normal chest roentgenograms, later had generalized rhonchi and radiologic evidence of partial collapse of the right upper lobe. The 21-year-old man, who did not have auscultatory abnormalities, was noted to have faint shadowing in the right lower lobe, which cleared within a few days.

The results of the pulmonary function studies are shown in Fig. 1. With the exception of one value for functional residual capacity and one each for total lung capacity and mid-expiratory flow rate the changes in pulmonary function were greater than two standard deviations from the mean of repeated measurements in 12 healthy subjects. Blood gas values, however, were normal on both occasions.

The 19-year-old pregnant woman delivered a term infant 26 days after exposure. The infant weighed 3500 g and had Apgar scores of nine at 1 and 5 minutes. No abnormalities were found by physical examination, and the infant remained well during a week in hospital.

Seven months after the incident we reassessed the three most severely exposed victims — the prospector and his two children. Although the father reported abnormal behaviour in the 7-year-old daughter, results of a physical examination were normal. Electroencephalograms, complete blood counts, liver function tests and analyses of 24-hour urine collections for protein content and creatinine clearance gave normal results for the three patients.

Serial blood mercury levels for the seven patients are plotted in Fig. 2. The average initial level (± one standard deviation) was 30.8 ± 1.5 μg/dl. The control blood samples had levels of less than 0.5 μg/dl. Data from the adults and children were plotted separately, as fewer points were available for the children, and they did not receive chelation therapy.

Computer analysis of the changes

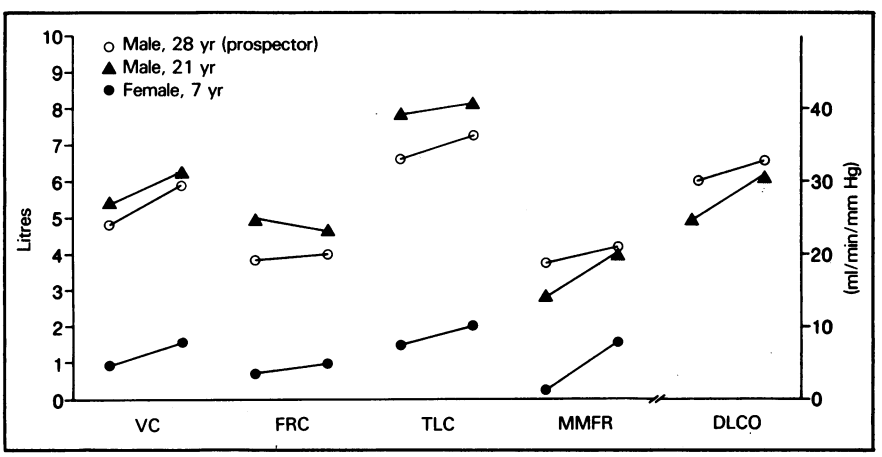

FIG. 1—Results of pulmonary function studies 2 and 40 days after accidental exposure to mercury vapour. VC = vital capacity; FRC = functional residual capacity; TLC = total lung capacity; MMFR = maximum mid-expiratory flow rate (per second); DLCO = diffusing capacity of the lung for carbon monoxide.

in blood mercury levels over time suggested that the data could be fitted without significant error by an equation involving two exponential terms. This implies that mercury in the blood behaves as a two-compartment system — the first compartment, with a half-life of approximately 2 days, containing a large amount of mercury and the second, with a half-life of 8 days, containing a smaller amount. In addition, there appeared to be a "bound fraction" from which there was no appreciable efflux during the time of measurement.

The oral administration of D-penicillamine from the 2nd to the 10th day after exposure did not have any apparent effect on the rate of decline of the blood mercury levels. The amount of mercury appearing in the urine at different times after exposure is shown in Fig. 3. While the data differed substantially from patient to patient, there was no evidence that mercury was excreted more rapidly during and after treatment with D-penicillamine than before therapy ($p > 0.05$).

The levels of mercury in the blood of the mother and her infant at birth and 6 days later are shown in Fig. 4.

Reassessment of the prospector and his two children 7 months after exposure revealed blood mercury levels of 1.57 to 1.76 μg/dl and urinary excretion levels for 24 hours of 9.8 to 11.9 μg.

Two days after the accident the premises were carefully inspected. Drops of mercury were seen on the stove top and burners, and the ambient mercury levels, measured with the windows open, varied from 0.12 mg/m³ around the stove to 0.04 mg/m³ in the basement suite. The measurements were repeated after 14 days, during which time the house had been cleaned but the windows had been kept closed. Values of up to 0.37 mg/m³ were obtained in the area of the stove. This necessitated removal of the stove and an extensive second cleaning. Mercury in the ambient air was not detected 45 days later.

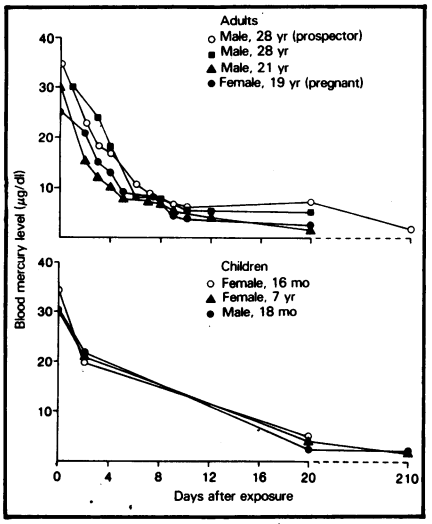

FIG. 2—Blood mercury levels of seven patients accidentally exposed to mercury vapour at various intervals after exposure.

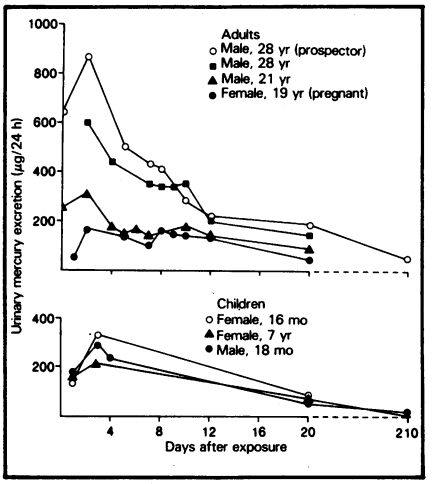

FIG. 3—Urinary mercury excretion at various intervals after exposure.

Discussion

The inhalation of mercury vapour produces a paroxysmal cough, dyspnea, substernal chest pain and tachypnea, all of which may increase in severity for several hours after exposure. There may also be intense nausea and vomiting. These symptoms, present in all seven of our patients, strongly resembled those of victims described previously.[1-7,11-14]

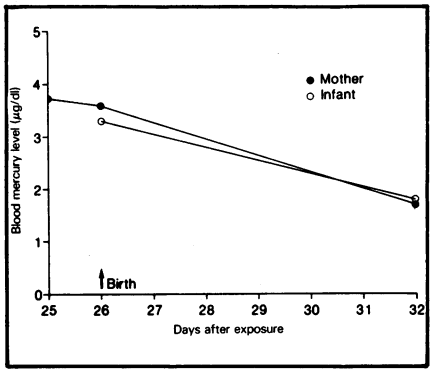

FIG. 4—Blood mercury levels in mother and infant born 26 days after exposure.

Mercury vapour acts as a direct airway irritant and a cellular poison.[15,16] In cases of mercury vapour inhalation in which death has occurred from respiratory failure, postmortem studies have shown severe damage to the bronchi and bronchioles, with marked alveolar edema.[4,12] In the presence of necrosis, complications such as interstitial emphysema, pneumomediastinum and pneumothorax can occur.[4,17]

Physiologic studies comparing the lung function in three of our patients 2 and 40 days after exposure reflected an initial loss of lung volume and diffusing capacity and airway obstruction. The values later improved to predicted levels. As might be expected, airway obstruction was most striking in the child with asthma. She also had partial atelectasis of the right upper lobe, from which she recovered in a few days.

The physiologic impairment in our patients strongly resembled that reported in four industrial workers exposed to mercury vapour.[1] The impairment probably reflects reversible changes at the sites at which more serious damage has been described in fatal cases.[4] Although short-term clinical recovery of lung function seemed complete in our cases, mild permanent damage from bronchiolitis obliterans cannot be excluded. Permanent changes from the acute inhalation of mercury vapour have been described in a man with persistent dyspnea who was found to have diffuse interstitial fibrosis at biopsy 5 months after exposure.[6]

Chest roentgenograms of patients exposed to mercury vapour may reveal pulmonary shadowing, probably caused by edema resulting from capillary damage. Although this is usually bilateral, the 21-year-old man had transient unilateral shadowing, which we attributed to this mechanism. Airway dysfunction is not detectable radiologically except indirectly as pulmonary hyperinflation in very severe cases.[4,17]

In addition to the severe lung damage that may occur as a result of mercury vapour inhalation, the lung also serves as a site from which mercury is well absorbed.[16,18] It is widely distributed throughout the body and passes across the blood–

brain barrier.[19] It is then largely ionized to mercuric ion in erythrocytes and other tissues.[15]

Within 24 hours after exposure the highest concentrations of mercury have been found in the kidney in animals studied experimentally and in humans.[4,12,13,16] However, a lack of correlation between the mercury content of the tissues and pathologic changes has been noted repeatedly.[20] Thus, the presence of mercury in the kidney does not usually manifest itself as overt clinical disease even though postmortem studies have frequently demonstrated cloudy swelling in the proximal tubules and diffuse swelling of the basement membranes.[4] In contrast, severe damage to the kidney may be produced by the ingestion of mercury salts, and the oral intake of elemental mercury has caused the nephrotic syndrome in children.[21] Two of the children in our series had a temporary reduction in creatinine clearance, a finding previously reported in workers exposed to mercury vapour.[22]

Mercuric ion is believed to be bound predominantly to sulfhydryl groups, although there is evidence that the other of its two valences may react with a nonsulfhydryl group.[23] Since sulfhydryl enzymes are plentiful in the body, mercury is potentially toxic to enzyme activity generally.[16]

Much of our data on mercury and its excretion is in accord with the more extensive experimental studies in the literature. We were able to demonstrate that mercury was excreted in our patients in two phases, the larger component having a half-life of 2 days and the smaller component a half-life of 8 days. Despite quantitative differences the results are similar to those of Hayes and Rothstein,[24] who studied mice exposed to mercury vapour. Like others,[25-27] we did not demonstrate an increased excretion of mercury after the administration of D-penicillamine. This failure is likely related to the relatively strong binding of inorganic mercury to the tissues in preference to D-penicillamine.[23,26] However, others have reported successful chelation, and the effectiveness of D-penicillamine therapy therefore remains unclear.[5]

Although a number of authors have advocated the use of N-acetyl-D,L-penicillamine,[28-30] this modified chelating agent is not currently available in North America. The effectiveness of other chelating agents, such as dimercaprol or calcium disodium edetate, is controversial.[5,6] Experimental data indicate that dimercaprol may augment the transfer of mercury into the central nervous system.[31]

Our data demonstrating similar blood levels in the mother and in her baby, born after exposure, suggest that mercury passes through the placenta to the fetus quite readily. These results agree closely with the observations of Clarkson and associates,[32] who found experimentally that inhaled mercury in rats is transported easily across the placenta. Despite the presence of significantly high blood mercury levels, the baby did not demonstrate any clinical abnormalities during the first few days of life. This outcome may be related to the time of exposure, as nearly all teratogens exert their effects during the period of organogenesis in the first trimester.

It is interesting that this single accident with mercury vapour contaminated the home so heavily with mercury. Despite cleaning, the environment remained affected for several weeks, until the stove was removed and extensive cleaning and renovations were carried out. The need for close monitoring and follow-up, as Sexton and colleagues[14] advocated, deserves re-emphasis.

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Apparent or true neonatal hip dislocation? Radiologic differential diagnosis

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A case of neonatal separation of the proximal femoral epiphysis secondary to obstetric trauma is presented. The radiologic differential diagnosis, as in other cases of neonatal dislocation of the hip, included congenital and septic dislocation of the hip and epiphyseal separation — so-called apparent dislocation. When clinical and laboratory signs are minimal or equivocal, x-ray films and, in difficult cases, contrast arthrograms are needed for an accurate diagnosis of neonatal dislocation of the hip.

On décrit un cas de séparation de l'épiphyse proximale du fémur chez un nouveau-né consécutive à un traumatisme obstétrical. Tout comme dans les autres cas de dislocation néonatale de la hanche, le diagnostic radiologique différentiel comprenait les luxations congénitale et septique de la hanche et la séparation épiphysaire, aussi appelée dislocation apparente. Quand les signes cliniques et les perturbations des épreuves de laboratoire sont minimes ou équivoques, une plaque simple et, dans les cas difficiles, un arthrogramme en contraste sont nécessaires pour établir un diagnostic précis de luxation néonatale de la hanche.

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When x-ray films show hip dislocation in the neonatal period before ossification of the femoral head there are three diagnostic possibilities: congenital, septic or apparent dislocation, the last existing when the cartilaginous femoral head and the acetabulum have a normal relationship but there is epiphyseal separation. Joint aspiration or arthrog-

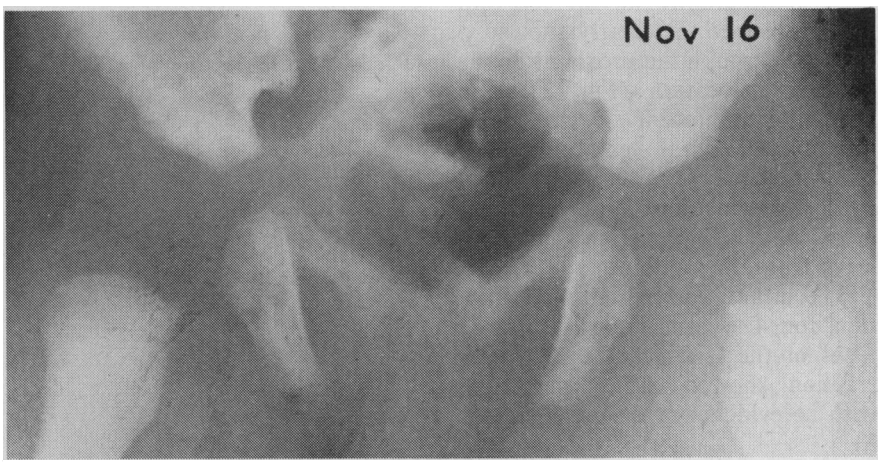

FIG. 1—Apparent dislocation of left hip in 6-day-old infant.

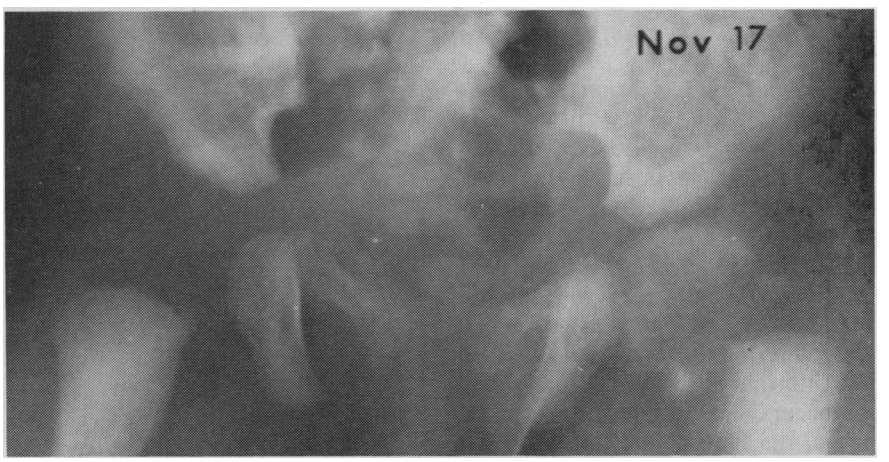

FIG. 2—Arthrogram shows no evidence of dislocation. Cartilaginous femoral head is well seated in normal acetabular fossa, but there is epiphyseal separation.